42. (Amended) A method of analysing the constructs of claim 1; the method comprising cleaving the construct at the first cleavage site to release the chemical fragment Fr, the cleavage reaction generating on the chemical fragment Fr at the cleavage site a group comprising a mass spectrometric sensitising group G (e.g. a group which is ionisable under mass spectroscopic conditions), and then subjecting the chemical fragment to mass spectrometry, e.g. electrospray mass spectrometry.

43. (Amended) An intermediate chemical construct for use preparing a chemical construct as defined in claim 1, the intermediate construct having the formula Q-Y' wherein Q' is a reactive or protected form of the group Q.

44. (Amended) An intermediate construct of the formula $Q\text{-}L^1\text{-}A^P$ wherein Q and L^1 are as defined in claim 1 and A^P is a reactive or protected form of the spacer group containing a peak splitting isotopic label.

REMARKS

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Applicants have attached an abstract on a separate sheet of paper as required by US practice. Applicants have amended the specification for purposes of adding the priority information. The claims have been amended to place them in form appropriate to US practice.

Respectfully Submitted,

Date: 4/5/2001

Frank P. Grassler
Registration No. 31,164

GlaxoSmithKline
Five Moore Drive
PO Box 13398
Research Triangle Park, NC 27709
Phone: 919-483-2482
Fax: 919-483-7988

Version with markings to show changes made

5. (Amended) A chemical construct according to [any one of] claim[s] 2 [to 4] wherein the means for imparting a characteristic signature to the mass spectrum of the fragment is located between the first and second cleavage sites.

6. (Amended) A chemical construct according to [any one of the preceding claims] claim 1 wherein the first and second cleavage sites cleavage sites are defined by first and second linker groups L^1 and L^2.

10. (Amended) A chemical construct according to [any one of the preceding claims] claim 1 wherein the sensitising group G is an ionisable group which is ionisable under mass spectrometric conditions.

12. (Amended) A chemical construct according to [any one of the preceding claims] claim 1 wherein the group G is a basic amino group.

17. (Amended) A chemical construct according to claim 12 [or claim 13] wherein the basic amino group is derived from the photochemical cleavage of a carbamate group.

18. (Amended) A chemical construct according to [any one of] claim[s] 3 [to 17] wherein the peak splitting isotopic label is contained within a substituted or unsubstituted alkylene diamine group.

21. (Amended) A chemical construct according to [any one of the preceding claims] claim 1 wherein the first cleavage site is selectively cleavable by one type of chemistry selected from a group of chemistries consisting of cleavage under acid conditions, base catalysed cleavage, oxidative cleavage, reductive cleavage, nucleophilic displacement, cleavage by 1,2 *bis* nucleophiles, electrophilic displacement, and thermal, photochemical and enzymatic cleavage, and the second cleavage site is selectively cleavable by a different type of chemistry selected from the said group.

24. (Amended) A chemical construct according to claim 21 [or claim 22] wherein the first cleavage site is defined by a sulphonamide linker group, and the second cleavage

site is optionally defined by a group, such as a Rink linker, which is cleavable under acidic conditions.

25. (Amended) A chemical construct according to claim 21 [or claim 22] wherein the first cleavage site is defined by a thiopyrimidine linker susceptible to cleavage by oxidation followed by nucleophilic displacement, and the second cleavage site is optionally defined by a group, such as a Rink linker, which is cleavable under acidic conditions.

26. (Amended) A chemical construct according to claim 21 [or claim 22] wherein the first cleavage site is defined by a dde group and the second cleavage site is optionally defined by a group, such as a Rink linker, which is cleavable under acidic conditions.

27. (Amended) A chemical construct according to claim 21 [or claim 22] wherein the first cleavage site is cleavable under photochemical conditions and the second cleavage site is defined by a group, such as a Rink linker, which is cleavable under acid conditions.

28. (Amended) A chemical construct according to claim 21 [or claim 22] wherein the first cleavage site is defined by a group such as allyloxycarbonylamino that can be cleaved by a transition metal such as palladium (0), and the second cleavage site is optionally defined by a group, such as a Rink linker, which is cleavable under acidic conditions

29. (Amended) A chemical construct according to claim 21 [or claim 22] wherein the first cleavage site is cleaved by oxidation followed by nucleophilic displacement.

32. (Amended) A chemical construct according to [any one of the preceding claims] claim 1 wherein the fragment Fr contains a chromophore C^u that facilitates analysis of the fragment Fr by ultraviolet, visible or fluorescence spectrophotometry.

35. (Amended) A chemical construct according to [any one of] claim[s] 1 [to 34], the construct comprising a solid support Q having linked thereto via the connecting group Y the substrate R wherein the fragment Fr comprises the substrate and at least a portion of the connecting group Y, and the said portion contains a chromophore C^u which facilitates analysis of the fragment Fr^u by ultra violet, visible or fluorescence

spectroscopy, the chromophore C^u having a principal log E_{max} value of at least 2.5 and wherein (i) the principal log E_{max} value is at least 1.5 times greater than the principal log E_{max} of the substrate R; or (ii) , the chromophore C^u has an absorption peak at a wavelength remote from absorptions due to the substrate R.

36. (Amended) A chemical construct according to [any one of] claim[s] 1 [to 35] comprising a solid support Q having linked thereto via the connecting group Y the substrate R wherein the fragment Fr comprises the substrate and at least a portion of the connecting group Y, and the said portion contains a chromophore C^u which facilitates analysis of the fragment Fr^u by ultra violet, visible or fluorescence spectroscopy, wherein the absorption characteristics of the chromophore C^u and the substrate R are such that at a given measurement wavelength, any errors in measurement of the quantity of substrate R (or any fragment or construct containing the fragment) arising from any overlap between absorption bands due to the chromophore and absorption bands due to the substrate R are less than 10%, preferably less than 5%.

37. (Amended) A chemical construct according to [any one of] claim[s] 32 [to 36] wherein the chromophore is a group containing an aryl group.

42. (Amended) A method of analysing the constructs of [any one of the preceding claims] claim 1; the method comprising cleaving the construct at the first cleavage site to release the chemical fragment Fr, the cleavage reaction generating on the chemical fragment Fr at the cleavage site a group comprising a mass spectrometric sensitising group G (e.g. a group which is ionisable under mass spectroscopic conditions), and then subjecting the chemical fragment to mass spectrometry, e.g. electrospray mass spectrometry.

43. (Amended) An intermediate chemical construct for use preparing a chemical construct as defined in [any one of the preceding claims] claim 1, the intermediate construct having the formula Q-Y' wherein Q' is a reactive or protected form of the group Q.

44. (Amended) An intermediate construct of the formula $Q\text{-}L^1\text{-}A^p$ wherein Q and L^1 are as defined in [any one of the preceding claims] claim 1 and A^p is a reactive or protected form of the spacer group containing a peak splitting isotopic label.